REMARKS

The invention currently claimed relates to purified nucleic acid sequences encoding AGE-1 polypeptides. The invention also relates to methods for the identification of compounds which decrease AGE-1 expression or activity.

Support for the Amendments

Applicants have amended claim 8 to recite a purified DNA which encodes an AGE-1 polypeptide having PI 3-kinase activity, at least 50% amino acid sequence identity to the full length polypeptide of Figure 6 (SEQ ID NO: 1), and a p85 domain and a lipid kinase domain. Applicants have also amended claim 9 to recite a purified DNA comprising an AGE-1 nucleic acid sequence which is at least 30% identical to the full length nucleic acid sequence of Figure 4 (SEQ ID NO: 2), and which encodes an AGE-1 polypeptide containing a p85 domain and a lipid kinase domain and having PI 3-kinase activity. Support for each of these amendments is found in the specification at page 2, lines 10-13, page 5, lines 7-26, and pages 21-22. The amendments of claims 16 and 20 find support in the specification at page 32, lines 8-21. Claim 18 has been amended to correct a typographical error. Support for new claims 29 and 30 is found in the specification at pages 1-2. No new matter has been added by these amendments.

Summary of the Office Action

Claims 8-13 and 16-20 stand rejected under 35 U.S.C. § 112, first paragraph. Claim 9 stands rejected under 35 U.S.C. § 112, second paragraph. Claims 8 and 9 stand rejected under 35 U.S.C. § 102(b). These rejections are addressed below in the order in which they appear in the Office Action.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 8 and 9 stand rejected under 35 U.S.C. § 112, first paragraph, based on the assertion that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Claims 8 and 9 also stand rejected on the basis that the specification is not enabling. These bases for the § 112 rejection are respectfully traversed.

Written Description

The adequate written description requirement of 35 U.S.C. § 112, first paragraph, provides that

> the specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...

The written description requirement serves "to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; how the specification accomplishes this is not material." *In re Wertheim*, 541 F.2d 257, 262, 191 U.S.P.Q. 90, 96 (C.C.P.A. 1976). In order to meet the written description requirement, the applicant need not utilize any particular form of disclosure to describe the subject matter claimed, but "the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989) (citation omitted). Stated another way, "the applicant must . . . convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention." *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991).

Claim 8, as amended, is drawn to a purified DNA which encodes an AGE-1 polypeptide having at least 50% amino acid sequence identity to the full length polypeptide of Figure 6 (SEQ ID NO: 1); the claimed polypeptide must include a p85 domain and a lipid kinase domain and must have PI 3-kinase activity. Claim 9 recites a purified DNA comprising an AGE-1 nucleic acid sequence which is at least 50% identical to the full length nucleic acid sequence of Figure 4 (SEQ ID NO: 2); again, the DNA encodes an AGE-1 polypeptide that includes a p85 domain and a lipid kinase domain and that has PI 3-kinase activity.

Applicants' specification clearly describes to the skilled worker what is claimed. Through Applicants' identification of the AGE-1 gene and the distinct characteristics of its encoded PI 3-kinase, Applicants have discovered what is a divergent PI-3 kinase class. Applicants' specification makes this clear. For example, at page 22 (lines 6-25), the specification describes the domains of AGE-1, including a lipid kinase domain and a p85 domain, and states the existence of this class.

Thus, there can be no question that Applicants were in possession of the claimed genus at the time their application was filed, and that one skilled in the art would recognize Applicants' disclosure as a description of the invention defined by the present claims. As a result, Applicants' specification clearly satisfies the written description requirement, as set forth by the case law, and Applicants request reconsideration and withdrawal of this basis for the § 112 rejection.

The rejection of claims 8 and 9, under 35 U.S.C. § 112, first paragraph, is also based on the assertion by the Office that the specification fails to provide a description of the other polypeptides present in a "substantially pure" preparation of AGE-1, or the nucleotides encoding those impurities. This basis for the rejection is respectfully traversed.

The Office Action states that the specification defines "substantially pure" as a preparation which is at least 60%, preferably at least 75%, more preferably at least 90%, and most preferably at lest 99% (dry weight) the compound of interest. From this

definition, the Examiner concludes that 1% to 25% of an AGE-1 preparation contains polypeptides of unknown nature. The Office Action then states that the specification provides no description of the polynucleotides that encode these impurities, and, on this basis, Applicants fail to satisfy the written description requirement.

In response to this rejection, Applicants contend that claims 8 and 9 are not directed to the impurities of a substantially pure preparation of AGE-1 polypeptide. Therefore, Applicants are uncertain as to why such a basis for a rejection is being made. Applicants submit that claims 8 and 9 satisfy § 112, first paragraph provided that Applicants describe the DNA encoding the AGE-1 polypeptide with 50% sequence identity to SEQ ID NO: 1 and the DNA having at least 30% nucleic acid sequence identity to SEQ ID NO: 2, respectively. The fact that a substantially pure preparation of AGE-1 polypeptide may contain impurities is irrelevant in view of recited claims 8 and 9, and Applicants respectfully request that this basis for the rejection be withdrawn.

Scope of Enablement

Claims 8-13 also stand rejected under 35 U.S.C. § 112, first paragraph, based on the statement in the Office Action that the specification is not enabling for the claimed invention because it does not provide sufficient guidance as to how an artisan would have made all the claimed polynucleotide sequences, vectors, and host cells expressing the sequences recited in claims 8-13. This rejection is respectfully traversed.

As noted above, claim 8, as amended, is drawn to a purified DNA which encodes an AGE-1 polypeptide having PI 3-kinase activity and possessing at least 50% amino acid sequence identity to the full length polypeptide of Figure 6 (SEQ ID NO: 1) as well as a p85 domain and a lipid kinase domain. Claim 9 recites a purified DNA which includes an AGE-1 nucleic acid sequence having at least 30% nucleic acid identity to the full length sequence of Figure 4 (SEQ ID NO: 2), where the DNA encodes an AGE-1 polypeptide which includes a p85 domain and a lipid kinase domain, and which exhibits PI 3-kinase activity.

Claims 10 and 11 recite a vector and cell, respectively, which include the AGE-1 DNA of claim 8 or 9. Claim 12 features a method of producing a recombinant AGE-1 polypeptide that involves providing a cell transformed with AGE-1 DNA, and expressing and isolating the AGE-1 polypeptide. And Claim 13 recites the recombinant AGE-1 polypeptide produced by the method of claim 12.

Claims 8 and 9 are specifically rejected based on the assertion that the specification does not provide guidance for how to make polynucleotides that encode AGE-1 polypeptides having at least 50% amino acid sequence identity to the polypeptide of SEQ ID NO: 1, or which have at least 30% sequence identity to the nucleic acid sequence of SEQ ID NO: 2. This basis for the rejection is respectfully traversed.

In response to this rejection, Applicants direct the Examiner's attention to pages 26-27 of the specification, where guidance for cloning mammalian AGE-1 polypeptides is provided. Although techniques for cloning mammalian homologs are commonly known to those of skill in the field of molecular biology, the specification nonetheless provides specific guidance for how mammalian AGE-1 polypeptides may be obtained using two different cloning strategies, hybridization cloning and PCR cloning. The specification provides exemplary AGE-1 sequences which may be used as the basis for probes or primers, and also directs the reader to references which describe primer and probe design. The specification further provides directions on how to use hybridization techniques, including high and low stringency hybridization conditions, and provides references for using such techniques to obtain mammalian AGE-1 clones. Furthermore, the specification provides references which may be used to clone AGE-1 genes by PCR cloning strategies. In view of these comments, Applicants assert that it would not require undue experimentation to obtain any number of mammalian or non-mammalian AGE-1 nucleic acid sequences, having Applicants' AGE-1 gene in hand.

Applicants further contend that, once a gene has been obtained using the above-described methods, it can be characterized using nothing more than routine techniques. For example, the sequence can very easily be analyzed using computer software programs which determine percent identity, to determine if the candidate gene encodes a polypeptide which has least 50% amino acid sequence identity to the full length

polypeptide of SEQ ID NO: 1, or at least 30% nucleic acid identity to the full length sequence of SEQ ID NO: 2. In addition, the DNAs can readily be examined using sequence analysis computer software to determine whether they encode polypeptides which possess lipid kinase and p85 domains (exactly as was done in Fig. 5 of the specification). Moreover, the polypeptides encoded by the DNAs of claims 8 and 9 can be assessed for PI 3-kinase activity using, for example, the standard methods referenced at page 32, lines 14-21. For example, methods for assaying PI 3-kinase activity include monitoring the ability of the enzyme to transfer ^{32}P-ATP to a PIP substrate on a TLC plate (as described, for example, by Whitman et al., *Nature* **322**:644-646, 1988), or the method of Kimura et al. (*J. Biol. Chem.* **269**:18961-18967, 1994) which involves the application of the PI 3-kinase inhibitor wortmannin and an assessment of PI 3-kinase activity by thin layer chromatography.

In view of these comments, Applicants submit that there is no reasonable scientific basis to support the Office's assertion that the present specification fails to enable one of skill in the art to obtain a reasonable number of DNAs recited in claims 8 and 9. This basis for the rejection may be withdrawn.

Claims 8 and 9 stand further rejected on the basis that the claimed DNAs do not encode AGE-1 polypeptides having any particular function. The Office Action states, "even if one had to assume that using various molecular biology techniques described in the specification at pages 26-27, and an artisan would have been able to make these

polynucleotides, would all the polypeptides encoded by the isolated polynucleotides have any specific function?" The Office further asserts that, just because the claimed polypeptides have amino acid identity to a known protein, this does not ensure that the polypeptide would have the function of an AGE-1 polypeptide. In view of the present amendment, this basis of the rejection may be withdrawn.

Applicants have amended claims 8 and 9 to specify that AGE-1 DNAs falling under the present claims encode polypeptides having PI 3-kinase activity. In view of these amendments, a DNA covered by claim 8 or 9 would, by necessity, have PI-3 kinase activity, and this basis for the rejection may be withdrawn.

The Office Action also focuses on the enablement of claims 10-13, stating that the specification does not provide sufficient guidance as to how an artisan would make a vector or a host cell containing the polynucleotide sequences of claims 8 and 9. The Office further states that the specification does not provide sufficient guidance for producing a recombinant AGE-1 polypeptide. These bases of the rejection are respectfully traversed.

Applicants assert that methods for making vectors containing a desired DNA sequence are well known in the art. For example, the specification at pages 28-29 describes expression systems for producing AGE-1 polypeptides. The specification references Cloning Vectors: A Laboratory Manual (P.H. Pouwels et al., 1985, Supp. 1987) for guidance in selecting an appropriate expression vehicle, and the insertion of an

AGE-1 DNA into such a vector is certainly routine in the art of molecular biology. Accordingly, Applicants submit that, given the guidelines provided in the specification and the level of skill in this art, one could readily generate a vector that includes a purified AGE-1 DNA, and this rejection may be withdrawn.

Likewise, Applicants submit that methods for making a cell that harbors the purified DNA of claim 8 or 9 are also widely known in the fields of molecular and cellular biology. Such a cell could readily be made using the information that was known in the art regarding generating transformed or transfected cells at the time the application was filed, particularly when used in conjunction with the guidance provided at pages 28-29 of the specification. There, the specification provides references for methods for generating prokaryotic or eukaryotic cells containing a desired gene. In one particular example, the specification references Ausubel et al. (*Current Protocols in Molecular Biology*, John Wiley & Sons, New York, N.Y.), a manual which provides detailed protocols for a variety of techniques for introducing DNA into a range of host cells. In view of this teaching, Applicants assert that, through a combination of the information provided in the specification, the state of the prior art, and the level of skill in the art, claim 11 is clearly enabled.

Responsive to the rejection of claims 12 and 13 under 35 U.S.C. § 112, first paragraph, Applicants contend that the specification, at pages 28-29, also provides methods for producing a recombinant AGE-1 polypeptide. There, methods for expressing

the polypeptide in a prokaryotic or eukaryotic expression system, as well as sources for expression vehicles and host cells and references for transformation and transfection methods are provided. The specification also provides an example of a mammalian expression system which can be used to produced an AGE-1 polypeptide, a DHFR expression system, and supplies optimal expression vectors and host cells for this system. The specification further states that expressed AGE-1 proteins may be isolated using affinity chromatography.

Moreover, Applicants submit that methods for the generation of recombinant proteins are routinely practiced in the field of molecular biology, and Applicants assert that this general knowledge in the art combined with the specification provides ample guidance for the production of a recombinant AGE-1 polypeptide. Applicants submit that claims 12 and 13 are enabled and request that this basis for the rejection be withdrawn.

Claims 16-20 also stand rejected under 35 U.S.C. § 112, first paragraph, based on the assertion that Applicants' specification does not enable the presently claimed AGE-1 screening methods. This rejection is respectfully traversed.

As amended, claims 16-20 are directed to methods of identifying compounds that decrease the PI 3-kinase activity of an AGE-1 polypeptide. These methods involve contacting a cell containing an AGE-1 polypeptide with a candidate compound and monitoring AGE-1 PI 3-kinase activity. This method may be carried out in an animal,

and the AGE-1 polypeptide may be from an animal. In addition, AGE-1 PI 3-kinase activity may be assayed *in vitro*.

The rejection of claims 16-20, under 35 U.S.C. § 112, first paragraph, is based on the following six grounds: (i) that the specification fails to provide any evidence relating to the activity of an AGE-1 polypeptide; (ii) that the specification fails to describe how an artisan would assay the activity of an AGE-1 polypeptide *in vitro* if the activity of the AGE-1 polypeptide is unknown; (iii) that the specification fails to provide any evidence that an AGE-1 polypeptide which has 50% identity with the peptide disclosed in SEQ ID NO: 1 would have the activity of an AGE-1 polypeptide; (iv) that the specification fails to provide guidance as to whether the AGE-1 polypeptide from animals would have the same activity as the AGE-1 polypeptide disclosed in SEQ ID NO: 1; and (v) that the specification fails to describe how an artisan would be able to carry out the claimed method in any animal or nematode. These bases for the rejection are respectfully traversed.

The first basis for the rejection turns on the assertion that the specification fails to provide any evidence relating to the activity of an AGE-1 polypeptide. This first basis for the rejection is respectfully traversed.

On this issue, the Examiner's attention is drawn to the specification at page 4, lines 15-16. There, Applicants state that the AGE-1 polypeptide is a PI 3-kinase. To more clearly define the invention, Applicants have amended claim 16 to specify that their

method identifies AGE-1 modulatory compounds by measuring decreases in AGE-1 PI 3-kinase activity. In view of the teaching in the specification and this amendment, specifying the activity of an AGE-1 polypeptide as a PI 3-kinase, this first basis for the rejection may be withdrawn.

The second basis for the § 112 rejection relates to the statement in the Office Action that the specification fails to describe how an artisan would assay AGE-1 activity *in vitro* if the activity of an AGE-1 polypeptide is unknown. This basis of the rejection focuses on the lack of sufficient guidance in the specification for determining whether the AGE-1 polypeptide must be purified from a crude extract in order to measure enzymatic activity, and whether an enzyme produced in a bacterial cell would be enzymatically active. This basis for the rejection is also respectfully traversed.

In view of the amendment to claim 16 reciting the function of an AGE-1 polypeptide as a PI 3-kinase, Applicants contend that the concerns of the Office Action regarding how an artisan could assay AGE-1 activity *in vitro* have been addressed. Specifically, it is now clear from the claims that the activity of an AGE-1 polypeptide is assayed *in vitro* by measuring PI 3-kinase activity, for example, according to the methods provided in the specification at page 32.

Regarding the issue of whether a candidate kinase must be purified in order to be assayed for kinase activity, Applicants contend that full purification is not required. Moreover, even if purified starting material were desired, Applicants' specification

provides guidance for purifying AGE-1 from a crude cell or tissue lysate using standard chromatography techniques. At page 29 of the specification, for example, Applicants describe affinity chromatography methods that would yield a polypeptide sufficiently pure for kinase activity measurements.

Applicants turn now to the Office's question of whether an AGE-1 polypeptide produced in a bacterial cell would be enzymatically active. In response to this question, Applicants first point out that the current claims are limited to the use of AGE-1 polypeptides that possess enzymatic — that is, PI 3-kinase — activity. Moreover, Applicants direct the Examiner's attention to pages 28-29 of the specification where methods for expressing AGE-1 polypeptides, in either prokaryotic or eukaryotic cells, are described. The specification recommends AGE-1 polypeptide production in prokaryotic cells because AGE-1 polypeptides do not require the type of post-translation modifications characteristic of eukaryotic cell expression. Accordingly, Applicants assert that the Office's concerns that the AGE-1 polypeptides of the invention would not be enzymatically active due to either impurities or insufficient post-translational modifications are unwarranted, and this basis of the rejection may be withdrawn.

The third basis for the § 112 rejection focuses on the assertion that the specification fails to describe whether a polypeptide which has 50% identity with the polypeptide disclosed in SEQ ID NO: 1 would have the activity of an AGE-1 polypeptide. This rejection is also respectfully traversed.

As stated above, Applicants have amended claim 16 to specify that their method of identifying an AGE-1 modulatory compound involves assaying PI 3-kinase activity. Accordingly, only polypeptides having such activity would fall within the claims, and this third basis for the rejection may also be withdrawn.

The fourth basis for the § 112 rejection involves the assertion in the Office Action that the specification fails to provide guidance as to whether an AGE-1 polypeptide from an animal would have the same activity as the AGE-1 polypeptide disclosed in SEQ ID NO: 1. This rejection is also respectfully traversed.

In response to this basis of the rejection, Applicants again point out that AGE-1 polypeptides covered by the current claims, for example, AGE-1 from any animal, are required to possess AGE-1 PI 3-kinase activity. In addition, Applicants direct the Examiner's attention to Hiles et al. (Cell 760:419-429, 1992). This reference provides evidence that bovine p110 has PI 3-kinase activity, supporting Applicants' position that AGE-1 polypeptides from animals possess such activity. Applicants respectfully request reconsideration on this rejection.

The final basis for the § 112 rejection regards the statement in the Office Action that the specification does not describe how the claimed screening methods may be carried out in any animal. This rejection is respectfully traversed.

In response to this basis for the rejection, Applicants assert that those skilled in research fields involving animal models readily understand how modulatory agents may

be tested in an animal. For example, those who work with nematode systems understand that an *in vivo* system for testing candidate AGE-1 antagonists involves providing two groups of nematodes, one which receives the candidate compound and one which receives vehicle only. Following contact of the nematodes with the compound or vehicle, AGE-1-specific effects are measured.

As described in the specification, one effect which can easily be assayed is the effect of the compound on dauer arrest, a function mediated by AGE-1. Ideal nematodes to be used in this screen are, for example, *age-1(hx546)* nematodes which are weak AGE-1 mutants, possessing maternal AGE-1 activity. As described in the specification at page 16, lines 14-20 and page 13, line 20 to page 14, line 7, *age-1(hx546)* nematodes demonstrate increased longevity, which is a result of decreased PI 3-kinase activity. If such animals are used to identify an AGE-1 antagonist, the effect measured is dauer arrest, because the maternal AGE-1 activity is inhibited. Specifically, in such a system, an AGE-1 antagonist results in the dauer arrest of the *age-1(hx546)* nematodes (compared to the *age-1(hx546)* nematodes receiving vehicle only).

Alternatively PI 3-kinase activity may be measured directly in nematodes receiving candidate modulatory compounds. A candidate compound which decreases PI-3 kinase activity (compared to the PI-3 kinase activity of nematodes receiving vehicle only) is identified as an AGE-1 antagonist.

In view of these assays for measuring AGE-1 activity, Applicants assert that the present specification provides sufficient guidance for carrying out AGE-1 modulatory compound screens in animals. Applicants respectfully request reconsideration and withdrawal of this final basis of the § 112 rejection.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 9 stands further rejected under 35 U.S.C. § 112, second paragraph, based on the claim term "percent identity." The Office Action states that it is unclear from the specification what parameters are used to calculate such identity, and that, on this basis, the claim is indefinite. This rejection is respectfully traversed.

Applicants point out that § 112, second paragraph does not require absolute metes and bounds for claim terms. Rather, the case law simply requires that a claim "reasonably apprise those skilled in the art both of the utilization and scope of the invention." *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q. 81 (Fed. Cir. 1986). In *Hybritech*, for example, the Federal Circuit reversed the district court's holding that claims directed to immunnoassays were indefinite because "antibody affinity cannot be estimated with any consistency." More specifically, the court found:

> [T]he evidence of record indisputably shows that calculating affinity was known in the art at the time of filing, and notwithstanding the fact that those calculations are not precise, or "standard," the claims, read in light of the specification, reasonably apprise those skilled in the art and are precise as the subject matter permits. As a matter of law, no court can demand more (emphasis added).

Id.

Applicants submit that claim 9 clearly meets this standard for definiteness under § 112, second paragraph. The calculation of sequence identity using standard formulas known in the art is no more difficult than the calculation of antibody affinities as discussed in *Hybritech,* where the court held the claims to be definite, despite finding that such calculations were "not precise, or 'standard.'"

Moreover, Applicants point out that, under § 112, second paragraph, the claims need not include a specific formula for calculating sequence identity as is apparently being required by the Office for claim 9. In particular, the Federal Circuit found such a requirement unnecessary in *Hybritech*, even though "there [was] no set of experimental conditions which [were] used to estimate [antibody] affinities." *Hybritech* at 1385. In this context, the Office's focus on the fact that there are different parameters which may be used to determine sequence identity is inappropriate for an analysis under § 112, second paragraph. Accordingly, in applying the case law to claim 9 and considering the routine nature of calculating sequence identities using standard computer software packages that were known when the application was filed, it is Applicants' position that one skilled in the art would be "reasonably apprised" of the scope of the claimed invention. Reconsideration on this issue is requested.

Rejections under 35 U.S.C. § 102(b)

Claims 8 and 9 are also rejected under 35 U.S.C. § 102(b) as being anticipated by Hiles et al. (Genbank Accession No. A43322; Cell 70:419-429, 1992), Goode et al. (Genbank Accession No. R46294; WO9403609-A), and Wilson et al. (Genbank Accession No. Z66519; Nature 368:32-38, 1994). This rejection is respectfully traversed.

Hiles et al. teach the nucleotide sequence of a 110 kD catalytic subunit of PI 3-kinase. According to the Office Action, the nucleotide sequence taught by Hiles shows 45.9% best local similarity to the claimed nucleotide sequence of SEQ ID NO: 2 (the nucleotide sequence of AGE-1), and the amino acid sequence shows 30.7% best local similarity to SEQ ID NO: 1 (the amino acid sequence of AGE-1).

Goode et al. teach eukaryotic cells transformed with mammalian phospholipid or protein kinase DNA, for use in assaying for compounds involved in cell growth regulation and treating cancer. According to the Office Action the amino acid sequence of Goode has 30.7% amino acid similarity with SEQ ID NO: 1, and the nucleotide sequence of Goode has 46% similarity with the nucleotide sequence of SEQ ID NO: 2.

Wilson et al. teach the complete sequence of *C. elegans* cosmid B0334, containing 2.2 MB of DNA from chromosome III of *C. elegans*. The Office Action asserts that within this 2.2 MB of sequence is a region which has 96% similarity to SEQ ID NO: 2

over a range of 150 nucleotides, and 100% sequence similarity in a region of 100 nucleotides.

Applicants note that the sequence analysis data (sent as part of the Office Action) does not compare the cited sequences to either the full length AGE-1 nucleotide sequence (SEQ ID NO: 2) or the full length AGE-1 amino acid sequence (SEQ ID NO: 1).

Claim 8, as amended, recites a purified DNA which encodes an AGE-1 polypeptide which has at least 50% amino acid sequence identity to the full length polypeptide of SEQ ID NO: 1. Applicants assert that, if the amino acid sequence of Hiles, Goode, or Wilson is compared to the full length AGE-1 amino acid sequence, each cited sequence would exhibit less than 50% similarity to the full length AGE-1 amino acid sequence of SEQ ID NO: 1. Therefore, Applicants submit that claim 8 is not anticipated by either Hiles, Goode, or Wilson and respectfully request that this rejection be withdrawn.

Claim 9, as amended, recites a purified DNA comprising an AGE-1 nucleic acid sequence which is at least 30% identical to the full length nucleic acid sequence of Figure 4 (SEQ ID NO: 2). Applicants contend that, if the nucleic acid sequence of Hiles, Good, or Wilson is compared to the full length sequence of SEQ ID NO: 2, the two sequences would be found to be less than 30% identical. Accordingly, Applicants submit that neither Hiles, Goode, nor Wilson anticipates claim 9 and respectfully request that this rejection also be withdrawn.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is respectfully requested.

Enclosed is a petition to extend the period for replying for three months, to and including February 17, 2000. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: 17 February 2000

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